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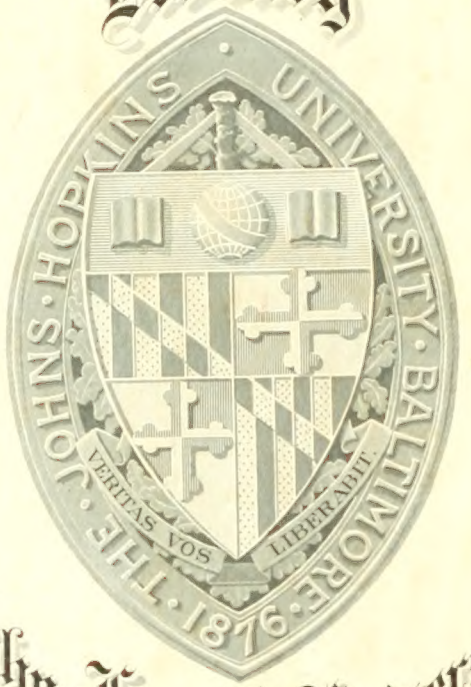

of the

Johns Hopkins University

The Phthaleins of Ortho-Sulpho-Para-Toluic Acid.

Dissertation

Presented to the Board of University Studies of the Johns Hopkins University for the Degree of Doctor of Philosophy.

by

James. A. Lyman.

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Acknowledgment.

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Historical and Introductory

A study of the sulphon-phthaleïns is necessarily patterned largely after the work of Baeyer, and a short sketch of the simple phthaleïns aids materially in following the formation of their more complicated sulphur analogues. An indication of what was to come was given in the reaction between phthalic anhydride and gallic acid, but the real development came this the study of the phthaleïns of phenol, resorcinal and pyrogallol.

When phenol acts upon phthalic anhydride, it was at first supposed that phenol phthaleïn was formed

1. Annalen, 202, 68.

according to the following reaction;-

$$C_6H_4\begin{matrix}CO\\CO\end{matrix}\!>\!O + \begin{matrix}H\\H\end{matrix}\!>\!C_6H_4OH = C_6H_4\begin{matrix}CO.C_6H_4OH\\CO.C_6H_4OH\end{matrix}\!> + H_2O$$

Subsequent evidence, however established the unsymmetrical formula for phthalidyl,

$$C_6H_4\begin{matrix}CH_2\\CO\end{matrix}\!>\!O$$

which is derived from phthalyl chloride. From this chloride di-phenyl-phthalide can be obtained, and this by appropriate reactions can be transformed into phenol phthaleïn. Much additional evidence has established the unsymmetrical formula for the phthaleins, phenol-phthaleïn having the structure

$$C\begin{cases}C_6H_4OH\\C_6H_4OH\\C_6H_4.CO\\O\text{——}\end{cases}$$

Resorcinol-phthaleïn or fluorescein,[2] hydroquinone-phthaleïn[3], and pyrogallol phthaleïn or gallein[4] have a similar general structure, but it has been shown that the anhydride condition exists between the residues of the phenols; pyrocatechin-phthaleïn[5], on the other hand, retains all its hydroxyl groups.

The phthaleïns as a class have strongly marked properties. All are brilliantly colored in alkaline solutions, and salts of the phenol-hydroxyl groups are formed. When treated with sulphuric acid, all yield derivatives of anthracene. By zinc dust and caustic potash they are reduced to colorless leuhalïns, a typical reaction being that with phenol-phthaleïn;-

$$C_6H_4\begin{cases}C(C_6H_4OH)_2\\CO\end{cases}O + H_2 = C_6H_4\begin{cases}CH(C_6H_4OH)_2\\COOH\end{cases}$$

2. Annalen, 183, 1. 3. Berichte, 6, 506.
4. Berichte, 4, 457, 555, 663; Annalen, 209, 249.
5. Berichte, 22, 2197

Historical references to the special sulphon-phthaleïns will be made later. The evidence collected goes to show that not only are there formed simple sulphur analogues but also more than two phenol-residues may enter into combination with the acid radicle, thus giving rise to more complex compounds.

Preparation of Ortho-sulpho para toluic Acid.- Para-toluic sulphimide or "methyl-saccharin" is the substance from which the acid is best prepared. The method devised by the "Badische Anilin- und Soda-fabrik" for the preparation of the sulphimide is as follows: Para-toluidine[1] is transformed into para-toluidine-meta-sulphonic acid by heating the acid sulphate[2]; by the Sandmeyer[3] reaction the amido group

1. Chem. Central-Blatt. 1887, 2, 795
2. Berichte, 13, 1947.
3. Ibid. 17, 2650.

is replaced by cyanogen, forming para-cyan-toluene-meta-sulphonic acid; from this by the action of phosphorus pentachloride the chloride is prepared, and from this the amide is made. By saponification with caustic soda solution this becomes ortho-sulphonamine-para-toluic acid, and on longer boiling this acid passes over into para toluic sulphimide. The successive products of these reactions are shown by the following formulae:-

$$C_6H_4\begin{cases}NH_2\ (1)\\ CH_3\ (4)\end{cases} \rightarrow C_6H_3\begin{cases}NH_2\ (1)\\ -SO_3H\ (2)\\ CH_3\ (4)\end{cases} \rightarrow C_6H_3\begin{cases}CN\\ -SO_3H\\ CH_3\end{cases} \rightarrow$$

$$C_6H_3\begin{cases}CN\\ -SO_2Cl\\ CH_3\end{cases} \rightarrow C_6H_3\begin{cases}CN\\ -SO_2.NH_2\\ CH_3\end{cases} \rightarrow C_6H_3\begin{cases}COOH\\ -SO_2.NH_2\\ CH_3\end{cases} \rightarrow C_6H_3\begin{cases}CO\\ -SO_2>NH\ (1)\\ CH_3\ (4)\end{cases}\ (2).$$

Ortho-sulpho-para-toluic acid was made from the methyl-saccharin that had

brew placed at the disposal of Prof. Remsen by the Badische Anilin- und Soda-fabrik, according to the method described by Randall,[1] who has investigated the properties of the acid. The methyl saccharin in portions of 25 grams was boiled in a flask fitted with a reflux condenser with a mixture of 100 c.c. of concentrated hydrochloric acid and 500 c.c. of water. Reaction took place, with the formation of the acid ammonium salt.

$$CH_3.C_6H_3\langle\begin{matrix}SO_2\\CO\end{matrix}\rangle NH + 2H_2O = CH_3.C_6H_3\langle\begin{matrix}SO_3NH_4\\COOH\end{matrix}$$

after boiling for two hours all the sulphinide had been transformed, and the solution was then decolorized and evaporated to crystallization.

The acid ammonium salt may by treatment with phosphorus pentachloride

1. Am. Chem. J., 13, No. 11.

be converted directly into the chloride of the acid; but as some of the chlor-phosphuret of nitrogen, $P_3N_3Cl_6$, is always formed,[2] it was found best to make the neutral potassium salt, from which the chloride was made. By boiling the chloride with water, ortho-sulpho-para-toluic acid is formed.

Notes:- Care must be taken that the orthosulphoparatoluic acid used in the preparation of phthaleïns is anhydrous, as the presence of water seems to promote the formation of tarry substances, preventing the obtaining of a pure product. The acid is best dehydrated by long heating below 135°, and is to be finely powdered before using.

The best method of analysis was

2. White, Dissertation, 1891.

found to be the burning in a platinum boat in a current of oxygen, the front half of the tube being filled with lead chromate. By the use of an open tube many successive combustions could be made with the least absorption of moisture from the air, and complete burning of the carbonized residue was assured. In two cases an appreciable amount of silica was left in the boat.

Action of Phenol.

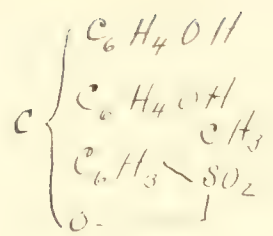
Phenol para-methyl-sulphon phthaleïn:- Carefully dehydrated ortho-sulpho para tolnic acid and dry, crystallized phenol in the proper molecular proportion — 1 to 2 — are heated together in a glass tube closed at one end. The glass tubing is used in preference to a test tube on account of its greater strength. The tube is held in a sulphuric acid bath by a clamp. It should be short enough to allow a ready escape of the water formed, without danger of the contents rushing over the top. As heat is applied to the bath, the contents of the tube melt to a colorless liquid, which grows pink as the temperature rises, and finally attains a

dark red at 150°, at which point it becomes opaque and a rapid evolution of water begins. More heat is slowly applied, until the thermometer in the tube indicates 170°, when the reaction goes on somewhat satisfactorily, while the contents are constantly stirred. After several hours the mass takes on a green lustre, and the thermometer leaves marks on the sides of the tube, as tho from the crushing of some crystalline body. Careful examination, however, failed to reveal anything, and the marks disappear presently. The evolution of water slackens as the mass grows viscous, and after heating for fifteen hours the contents of the tube are nearly solid. The thermometer is then taken out and the tube allowed to cool, when the contents usually break

loose and can be readily removed.

When the reaction has proceeded properly, the product is a black, resinous solid showing a green lustre. It was powdered and washed with hot water to remove any phenol and ortho-sulpho-para-toluic acid remaining. Next it was dissolved in caustic potash, precipitated from it's hot solution with hydrochloric acid and washed with hot water until no test for chlorine was obtained with silver nitrate. The precipitate becomes more compact on boiling with water. It was dried by long standing in a desiccator over sulphuric acid.

Analogy with phenol-phthalein would lead to the supposition that a similar compound had been formed, having this structure:-



Analysis showed that such was the fact.

I. 0.5552 gram substance gave 0.3207 gram $BaSO_4$.

II. 0.2080 gram substance gave 0.1197 gram $BaSO_4$.

III. 0.~~1820~~ .1790 gram substance gave 0.0809 gram H_2O and 0.3724 gram CO_2.

IV. 0.~~2025~~ .1772 gram substance gave 0.~~0851~~ gram H_2O and 0.4154 gram CO_2.

	Calculated for	Found			
	$C_{20}H_{16}O_5S+3H_2O$	I.	II.	III.	IV.
C	56.87	-	-	56.~~75~~	56.88
H	5.21	-	-	5.02	4.91
S	7.59	7.94	7.91	-	-

An attempt was made to determine the water given off on heating, but when

a loss had taken place closely approximating that required by the above formula, traces of hydrogen sulphide were given off and the attempt was abandoned. This phenomenon has been noted by White in his investigation of sulphon fluorescein.[1]

Pure diphenol-para-methyl-sulphonphthaleïn is not always obtained by the process just described, and an attempt to purify a mixed product was made, based on the solubility in water. After thorough washing, the substances were treated with large quantities of boiling water and filtered hot. The orange solution was evaporated to dryness on the water-bath and a product was obtained having the same properties as the pure di-phenol derivative. Analysis

[1] White, Dissertation, 1871, p. 19.

showed their identity, except that the product last obtained contained less water, as might be expected from its manner of preparation.

I. 0.2641 gram substance gave 0.1126 gram H_2O and 0.5854 gram CO_2.

II. 0.4167 gram substance gave 0.2340 gram $BaSO_4$.

	Calculated for $C_{20}H_{16}O_5S + 1\frac{1}{2}H_2O$	Found I.	Found II.
C	60.75	60.45	
H	4.81	4.74	
S	8.10		8.37

Phenol-para-methyl-sulphon-phthaleïn is a dark-red, amorphous powder, slightly soluble in alcohol, ether, and chloroform, and in warm glacial acetic acid. When these solvents are heated

a larger quantity dissolves, which on cooling comes down as a flaky precipitate. In alkaline carbonates, more readily in caustic alkalies, it dissolves to a red liquid, almost black in strong solution. It shows a striking purple-red in dilute form which changes to yellow on the addition of acids, suggesting its possible use as an indicator. The purple color is not affected by exposure to the air even for a long period of time.

All attempts to obtain a crystalline product by the use of the ordinary solvents were failures, as only brown flakes, neutral, but the use of a solution in water containing a little phenol was attended with better success. A clear, filtered solution was obtained, and, as nothing was deposited, the vessel

containing it was covered with a watch-glass and allowed to stand in a sheltered place for several weeks. After some time, examination showed the presence of groups of short, yellow prisms floating from the surface of the liquid. Further evaporation caused these groups to grow, tho the crystals always remained very small. When exposed to the air they took on a great lustre. Their crystal character was not examined, as it was impossible to keep them in their original form after removal from the solution. The amount was too small for complete analysis. So far as is known, this is the only case of a crystallized sulphonaphthalein yet noted.

Action of bromine on phenol para-methyl-sulphon phthaleïn:- The substance was treated with the theoretical amount of bromine required to form a di-brom substitution-product. The bromine used was in the form of a twenty percent solution in glacial acetic acid and was poured upon the sulphon-phthaleïn suspended in glacial acetic acid in a small Erlenmeyer flask. Reaction at once took place, accompanied by the production of heat and the evolution of fumes of hydrobromic acid. After standing a short time the whole was heated for half an hour on the water-bath and filtered thrò glass wool. A small residue of unchanged phthaleïn was left on the filter. As the addition of water failed to produce any considerable

precipitate, the solution was evaporated to dryness on the water-bath, and the residue was powdered and placed in a dessicator over caustic potash. The product thus obtained was a light brown powder, soluble to a considerable extent in water. In alkalies it dissolves to a deep blue solution, showing greenish against a white background; the solution stains the skin a persistent blue, which acids change to a light yellow. A determination of bromine gave the following result;-

	Calculated for $C_{20}H_{14}Br_2O_5S$.	Calculated for $C_{20}H_{13}Br_3O_5S$	Found I.
Br	32.32	39.59	35.99

A second preparation was analyzed for bromine and sulphur;-

I. 0.2152 gram substance gave 0.1954 gram $AgBr$.

II 0.2400 gram substance gave 0.0801 gram $BaSO_4$.

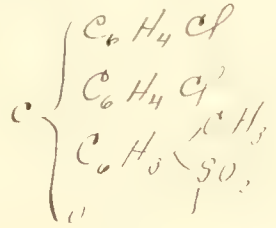
	Calculated for	Found	
	$C_{20}H_{13}Br_3O_5S$	I.	II.
Br	37.57	38.64.	
S	5.29	-	4.59.

It seems, then, that a tri-brom substitution-product is formed; but, owing to the difficulty of separating it from the unchanged phthaleïn and from other substitution-products it was not obtained in a perfectly pure form. Treatment with other proportions of Bromine gave similar impure tri-brom derivatives.

Action of Phosphorus pentachloride on Benzoyl-para-methyl sulphon pitbaline:

When the substance is treated in a small Erlenmeyer flask with a small excess of phosphorus pentachloride, slight reaction takes place at once, perhaps with the decomposition of the water contained, and the mass becomes somewhat coherent, but after this first action nothing further takes place. Accordingly the flask was heated to 130° in a sulphuric acid bath, when the mass melted and a lively effervescence followed. The heating was continued until all action had ceased. The product was a dark red liquid that became viscous on cooling. When treated with cold water, it slowly fell to an insoluble pink powder.

The most natural expectation would be that a product had been formed of this structure:-



The substance obtained, however, does not exhibit the properties of such a compound. It does not go into solution, even when boiled with strong caustic potash, but is apparently subjected to a deeper decomposition, forming a turbid liquid with the potash and giving off a phenol-like odor. Analysis of a specimen gave the following results;-

I. 0.1751 gram substance gave 0.0627 gram H_2O and 0.3005 gram CO_2.

II. 0.1607 gram substance gave 0.0516 gram H_2O

and 0.2753 gram CO_2.

III. 0.2567 gram substance gave 0.0511 gram $BaSO_4$.

IV. 0.1796 gram substance gave 0.0356 gram $BaSO_4$.

V. 0.1999 gram substance gave 0.0382 gram $BaSO_4$.

VI. 0.2087 gram substance gave 0.2337 gram AgCl.

VII. 0.2408 gram substance gave 0.2703 gram AgCl.

	Calculated for $C_{20}H_{14}O_2SCl_4$	Calculated for $C_{20}H_{14}O_2SCl_4+3H_2O$	Found					
			I.	II.	III.	IV.	V.	VI.	VII.
C	52.23	46.74	46.80	46.72	-	-	-	-	-
H	3.05	3.87	3.97	3.63	-	-	-		
S	6.96	6.23	-	-	2.74	2.72	2.63	-	
Cl	30.79	27.55	-	-	-	-	-	27.68	27.75

The low percentage of sulphur, would indicate that some deep seated change had taken place. A compound having approximately the composition found would have the formula $C_{46}O_{14}H_{44}SCl_9$; it would thus be formed from three

molecules of the phthalein by some process of condensation, an anthracene derivative being perhaps formed, as is the case when phenol-phthalein is treated with sulphuric acid; but the reaction in this case is evidently different from that in any cases heretofore noted.

Tetra-phenol para methyl-sulphon-phthalein:— When one molecule of ortho-sulpho-para-toluic acid is treated with four molecules of phenol, reaction at first proceeds as in the formation of the di-phenol-derivative; but after some hours' heating, the mass changes in color, becoming a brown, tar-like substance that will not solidify even after prolonged heating and is partially insoluble in alkalies, giving with them a cloudy, red-brown solution. Proportions of one to

six act in the same way. No analysis was made.

When the acid is heated with phenol in the proportion of one to two, as has been said, the usual product is the formation of the di-phenol derivative. But, from some unknown cause, the reaction often takes a different turn and a mixture of the di-phenol and the tetra-phenol derivatives is obtained; and occasionally a pure tetra-phenol compound is formed, as analytical results show:

I. 0.2244 gram substance gave 0.1148 gram H_2O and 0.5392 gram CO_2.

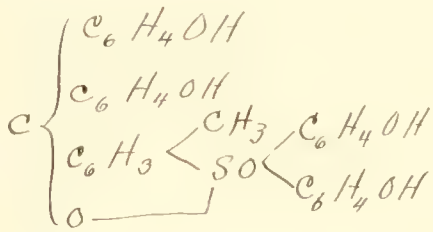
II. 0.1613 gram substance gave 0.0765 gram H_2O and 0.3862 gram CO_2.

III. 0.1057 gram substance gave 0.0392 gram $BaSO_4$.

IV. 0.1239 gram substance gave 0.0521 gram $BaSO_4$.

	Calculated for	Found			
	$C_{32}H_{26}O_6S + 2\frac{1}{2}H_2O$	I.	II.	III.	IV.
C	65.86	65.50	65.28		
H	4.80	5.07	4.71	–	–
S	5.49	–	–	5.09	5.77

The amount of water lost at 120° corresponded to 1½ molecules. At a higher temperature the remaining molecule of water is gradually lost, and at 200°, where the substance begins to soften, nearly all required by the theory is lost. The following may be given as the probable structure of the compound:-



The substance is a dark-red powder

having properties similar to those of the di-phenol derivative. It dissolves in alkalies with a purple-red color, and is again precipitated by acids as a brown, flocculent mass that becomes compact on boiling. It is slightly soluble in water, - less so than the other phthaleïn obtained. Zinc dust and caustic potash quickly reduce it to a yellow solution, which soon oxidizes again. With bromine it gives compounds blue in alkaline solution, but these were not studied.

Action of phosphorous pentachloride on tetra-phenol para methyl sulphon-phthaleïn. The phthaleïn was treated in precisely the same manner as was di-phenol-para-methyl-sulphon phthaleïn, the final product being a heavy dark-red

powder, soluble to a considerable extent in alcohol and ether, but entirely insoluble in water. Alkalies dissolve it on boiling, and from the solution something different is precipitated by acids. Analysis gave the following results;

I. 0.1895 gram substance gave 0.0386 grams $BaSO_4$.

II. 0.2302 gram substance gave 0.2445 gram $AgCl$.

	Calculated for $C_{32}H_{21}OCl_6S$	Calculated for $C_{32}H_{22}O_2Cl_4S$	Found I.	Found II.
S.	4.81	5.23	2.80	—
Cl	31.90	23.15	—	26.26.

The amount of sulphur indicated that some condensation had taken place, as in the case of the di-phenol product.

Other phenol-compounds;- Several other phenol compounds or mixtures of such

were obtained. One of these was made from a specimen of ortho-sulpho-para-tolnic acid that had melted during the process of dehydration. One molecule of the acid heated with two molecules of phenol gave after fifteen hours' heating a solid compound rather easily soluble in water and giving with alkalies a solution carmine in color when concentrated. The color was markedly different from that of the other compounds described. Analysis failed to throw any light on its structure.

I. 0.3016 gram substance gave 0.1136 gram $BaSO_4$.

II. 0.2044 gram substance gave 0.0786 gram $BaSO_4$

III. 0.1541 gram substance gave 0.0667 gram H_2O and 0.3940 gram CO_2.

IV. 0.1649 gram substance gave 0.0703 gram H_2O and 0.4225 gram CO_2.

Found

	I.	II.	III.	IV.
C	–	–	69.73	69.92
H	–	–	4.76	4.74
S	5.17	5.28	–	–

Action of Pyrocatechin.

To make a pyrocatechin-sulphon-phthaleïn, one equivalent of ortho-sulpho-para-toluic acid was heated with two equivalents of pyrocatechin in the usual way. Vigorous reaction took place, accompanied by a copious evolution of water, and the whole mass soon became viscous and clung to the sides of the tube. After two hours of heating at a temperature of 165°, the

reaction was completed, the substance being a black, friable mass. With water it became somewhat gelatinous and entirely prevented filtration. It was accordingly evaporated to dryness and powdered, when it still presented some of the same difficulties; but the washing was finally completed with a considerable loss of substance.

Analysis showed surprising results.

I. 0.1000 gram substance gave 0.0203 gram $BaSO_4$.

II. 0.1280 gram substance gave 0.0246 gram $BaSO_4$.

III. 0.1172 gram substance gave 0.0468 gram H_2O and 0.2897 gram CO_2.

IV. 0.1477 gram substance gave 0.0632 gram H_2O and 0.3569 gram CO_2.

	Calculated for $C_{20}H_{16}O_7S$ (2 mol. pyrocatechin)	Calculated for $C_{44}H_{30}O_{10}S + 2H_2O$ (6 mol.)	Calculated for $C_{56}H_{38}O_{12}S + 3\frac{1}{2}H_2O$ (8 mol)	Found I	II	III	IV
C	60.00	67.17	67.40	-	-	67.42	67.20
H	4.00	4.32	4.51	-	-	4.44	4.75
S	8.00	4.07	3.21	2.79	2.73	-	-

The results of analysis seem to agree best with the requirements of a compound containing eight residues of pyrocatechin. The the percentages of carbon and hydrogen agree nearly as well with a hexa-pyrocatechin derivative, the percentage of sulphur points to the former compound. The formation of an octo-derivative would not be an isolated case; a similar compound of resorcin I will presently be described, and its character can better be discussed then. But it is unexpected, that such a compound should be formed with the proportions used. It is to be regretted that the loss involved in its preparation left so little of the substance that its more detailed study was impossible. The compound is a black powder dissolving in alkalies with an evanescent grass-green color.

Action of Resorcinol.

Sulphon-fluorescein, the sulphur analogue of fluorescein, has been the subject of several investigations. In 1884 Remsen[1] obtained a fluorescent substance on heating ortho sulpho-benzoic acid with resorcinol. Three years later, by use of the same substances Remsen and Hayes[2] obtained a product that they analyzed, the results leading them to ascribe to it the formula of the theoretical sulphon-fluorescein, but Remsen and Linn[3] shortly after showed that the supposed ortho-sulpho-benzoic acid was really the acid ammonium salt of that acid, the substance obtained being the acid ammonium salt of dioxybenzoyl benzene-sulphonic acid. From this

1. Am. Chem. J., 6, 180. 2. Ibid., 9, 372.
3. Ibid, 11, 73.

latter acid the obtained sulphon-fluorescëin, as Baeyer obtained fluorescëin from dioxy-benzoyl-benzoic acid on heating.

White in his Dissertation, (1891,) gives the results of an investigation of sulphon-fluorescëin. After preparing the substance by the method just cited, he studied its reactions; among them the action of bromine, which yields, as a tetra-brom-substitution-product like fluorescëin, but a di-brom-product. Treatment with phosphorus pentachloride gives a tetra-chloride. The result of the treatment of ortho sulpho benzoic acid with different proportions of resorcinol is interesting. According to Fahlberg and Barge[4], when the two substances are heated in the proportion of one to two or one to four molecules, a product is obtained

4. Berichte, 22, 765

containing four resorcinol residues. White found that when the proportion of one to two was used, a tetra-substitution-product resulted, while the use of the proportions one to four or one to six gave a substance containing six resorcinol residues. A series of three resorcinsulphonphthaleïns was thus obtained.

The resorcinol phthaleïns of ortho-sulpho-para-toluic acid have been made by Jones in his dissertation, 1891. Para methyl sulphonfluorescëin was made by heating para-methyl dioxy benzyl benzene sulphonic acid, and chlorine and bromine compounds were made similar to those of sulphonfluorescëin. It was also found that heating together ortho-sulpho-para-toluic acid and resorcinol in the proportion of one to two gave a tetra-

resorcinol compound, while the proportions one to four and one to six gave a compound containing six resorcinol residues. Thus in this case also a series of three methyl-sulphon-phthaleïns was obtained. As the hexa resorcinol-derivative was manifestly impure, it seemed advisable to repeat the experiment, with the object of obtaining a pure product.

Treatment of ortho-sulpho para toluic acid with various proportions of resorcinol:- One equivalent of the acid was heated with two equivalents of resorcinol. The latter melted and dissolved the acid, forming a red liquid. Reaction began at 150°, and the mass was allowed to remain at 170° for about two hours. It gradually grew stiff, and on cooling was a brittle

black solid giving a dark red powder. It was purified in the usual way. In water it dissolved slightly with a yellow color, and with alkalies it gave the characteristic red-green fluorescence. A determination of sulphur was made.

	Calculated for $C_{20}H_{14}O_6S + H_2O$ (2 mol.)	Calculated for $C_{32}H_{22}O_8S + 3H_2O$ (4 mol)	Found
S	8.39	5.17	5.86

The result indicates that an impure tetra-resorcinol-derivative had been formed.

When ortho-sulpho-para-toluic acid and resorcinol in the proportions of one to four were heated together, reaction was completed in about two hours, the product being a very brittle black

substance having properties similar to those of the substance just described. Determinations of sulphur in the washed product were made.

I. 0.2028 gram substance gave 0.0634 gram $BaSO_4$.

II. 0.3122 gram substance gave 0.0973 gram $BaSO_4$.

	Calculated for $C_{44}H_{30}O_{10}S + 4H_2O$ (6 mols.)	Calculated for $C_{44}H_{30}O_{10}S + 3H_2O$	Found I.	Found II.
S	3.90	3.98	4.30	4.28

A fairly pure hexa-resorcinol-derivative was thus obtained; but the compound was made in a pure form by the use of other proportions.

Hexa-resorcinol para-methyl-sulphon-phthaleïn:- Ortho-sulpho para-toluic acid and resorcinol in the molecular proportion of one to six were heated

together in a short tube. At 150° vigorous reaction began, and the temperature was allowed to rise slowly, with constant stirring by the thermometer, until 170° was indicated. At the end of five hours the almost solid mass was allowed to cool. It was, like the other resorcin compounds, a brittle, black mass, showing electrical properties. When powdered and placed in water, it softened and then grew hard again, forming brown, brittle grains. It was twice dissolved in caustic potash, precipitated with hydrochloric acid, and washed on the filter.

The product is a dark-red powder, rather difficult to handle when dry, as it becomes electrified when stirred. It dissolves in water to a slight extent, giving a bright, yellow

solution with a tendency to fluorescence.
When boiled with water it becomes compact. It dissolves at once in alkalies, less readily in alkaline carbonates, giving a red solution showing a strong green fluorescence, which, when diluted, becomes pink with green.
On standing in alkaline solution for several days, a reddish precipitate settles out, and the color becomes less intense. Zinc dust and caustic potash reduce it to a yellow solution; this, when filtered, quickly oxidizes again. It is slightly soluble in alcohol and ether and in warm glacial acetic acid. Hot water containing resorcinol dissolves a considerable quantity, which on cooling separates as a fine powder. It tends to crystallize the substance

were unsuccessful. The results of analysis are as follows;-

I. 0.2928 gram substance gave 0.0830 gram $BaSO_4$.

II. 0.2197 gram substance gave 0.0622 gram $BaSO_4$.

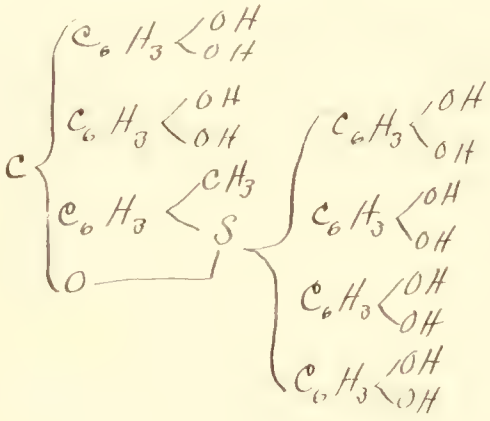
III. 0.1507 gram substance gave 0.0640 gram H_2O and 0.3623 gram CO_2.

IV. 0.1668 gram substance gave 0.0703 gram H_2O and 0.4011 gram CO_2.

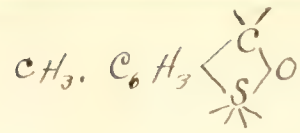
	Calculated for $C_{44}H_{30}O_{10}S+4H_2O$ (Jones)	Calculated for $C_{44}H_{30}O_{10}S+3H_2O$ or $C_{44}H_{36}O_{13}S$.	Found I.	II.	III.	IV.
C	64.21	65.67	-	-	65.36	65.59
H	4.63	4.48	-	-	4.71	4.67
S	3.90	3.98	3.90	3.89	-	-

It seems more likely that the compound contains three molecules of water than four. Whether this so-called water exists as such or as hydroxyl in

the resorcinol residues could not be determined. Attempts to drive off this amount of water by heating were unsuccessful, the substance melting at 200° before any loss corresponding to three molecules of water had occurred. The following may be given as the probable structure:-



Action of eight molecules of resorcinol on ortho sulpho para-toluic acid:- It will be noted that in the formula above given, all the oxygen atoms have been replaced, except the connecting anhydride atom;



The question is at once suggested, can this remaining oxygen atom be replaced by phenol residues? It differs from the other atoms of the same element, in that it exercises a linking function; but in the case of pyrocatechin it has been seen that there is a possibility of its replacement. In view of the ready action of both resorcinol and ortho-sulpho para tolnic acid in the formation of phthaleins, a favorable opportunity is here presented for investigating the possibility.

Ortho-sulpho-para tolnic acid and resorcinol, one molecule of the former to eight of the latter, were heated together in the usual manner. Reaction readily took place, about ten hours being

required for its completion. The product was a stick of brittle, black material, solid up to 200°, and exhibiting a radiating structure when broken. If rubbed, it exhibited electrical properties; and when powdered and thrown upon water it at first softened and then hardened to a friable mass. It was washed with warm water, and then twice dissolved in caustic potash and reprecipitated by hydrochloric acid, being each time filtered and washed. It was finally dried by long standing in a dessicator. Two determinations of sulphur were made.

I. 0.2485 gram substance gave 0.0594 gram $BaSO_4$.

II. 0.2836 gram substance gave 0.0658 gram $BaSO_4$.

	Calculated for (6 mol.) $C_{44}H_{36}O_{13}S$	Calculated for (8 mol.) $C_{56}H_{46}O_{16}S$	Found I.	Found II.
S	3.98	3.18	3.29	3.19

As only a small quantity of the compound had been made, a complete analysis had not been attempted. Accordingly a second preparation was made, using larger quantities. This product was in every way similar to the one first obtained.

I. 0.1727 gram substance gave 0.0696 gram H_2O and 0.4238 gram CO_2.

II. 0.1660 gram substance gave 0.0677 gram H_2O and 0.4065 gram CO_2.

III. 0.1547 gram substance gave 0.0628 gram H_2O and 0.3805 gram CO_2.

IV. 0.1298 gram substance gave 0.0524 gram H_2O and 0.3174 gram CO_2.

V. 0.2197 gram substance gave 0.0495 gram $BaSO_4$.

	Calculated for	Found				
	$C_{56}H_{46}O_{16}S$	I.	II.	III.	IV.	V.
C	66.80	66.86	66.75	67.07	66.69	-
H	4.57	4.48	4.53	4.52	4.49	
S	3.18	-	-	-	-	3.10.

A third product, similar to the other two, was made and analyzed.

I. 0.1543 gram substance gave 0.0625 gram H_2O and 0.3771 gram CO_2.

II. 0.2426 gram substance gave 0.0570 gram $BaSO_4$.

III. 0.2629 gram substance gave 0.0626 gram $BaSO_4$.

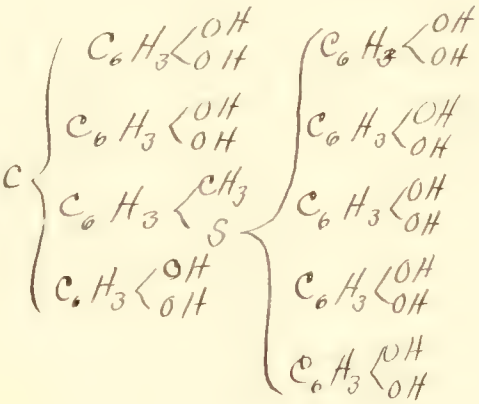
	Calculated for	Found		
	$C_{56}H_{46}O_{16}S$	I.	II.	III.
C	66.80	66.71	-	
H	4.57	4.50	-	-
S	3.18	-	3.23	3.27

No other phthaleïn that could be formed agrees with the percentage composition found. The following is the average of all the determinations made, compared with the composition of various phthaleins:-

	Average found	$C_{56}H_{46}O_{16}S$ (8 mol.)	$C_{44}H_{30}O_{10}S.3H_2O$ (6 mol.)	$C_{44}H_{30}O_{10}S.2H_2O$ (6 mol.)
C	66.81	66.80	65.67	67.17
H	4.50	4.57	4.48	4.32
S	3.21	3.18	3.98	4.07

The coïncidence between the first two columns is striking. Supposing that the anhydride condition exists between the pairs of resorcinol residues, the formula of the substance might be written $C_{56}H_{38}O_{12}S + 4H_2O$, but attempts to drive off four molecules of water were unsuccessful, the substance becoming viscous

above 200°. The probability, then, is that no anhydride condition exists, and that the following is the structure of the substance.



Phthaleïns, by warming with zinc dust and caustic potash, are reduced to phthalins.[1] Now if the structure above given be the true one, there is no opportunity for the formation of a phthalin in the case under consideration, all the oxygen atoms being replaced, and a possible method of testing it is suggested. As a matter of fact,

[1] See page 3 for the reaction.

reduction, or at least loss of color, does take place, but only after long boiling with the reducing agent and then in such a manner as to suggest that a decomposition had taken place. The evidence from this source is indecisive. The formation of pure derivatives was not satisfactorily accomplished, so that the analyses given and the proofs on which belief in the existence of the substance is based. There is no good reason, so far as known, why a sulfophthaleïn containing eight residues of resorcinol should not be formed; that a compound having the empirical formula $C_{56}H_{46}O_{16}S$ is produced is shown by the analysis of three distinct specimens, and it is difficult to see how the structure could be

different from that given. But further proof from the study of its derivatives and of analogous compounds is required, before its existence can be asserted without reservation.

Action of phosphorus pentachloride on octo-resorcinol para methyl sulphon phthaleïn:- The phthaleïn just described was treated with phosphorus pentachloride sufficient to decompose the hydroxyl groups. After heating for a short time at 130° until action had ceased, there resulted a stiff, purple mass that with water gave a brown, insoluble powder. This powder was slightly soluble in boiling alkaline liquids, giving a yellow color; but an insoluble residue always remained. Analysis showed that some decomposed

change had taken place.

I. 0.2064 gram substance gave 0.2429 gram $AgCl$.

II. 0.1795 gram substance gave 0.0268 gram $BaSO_4$.

III. 0.1839 gram substance gave 0.0287 gram $BaSO_4$

IV. 0.1691 gram substance gave 0.0575 gram H_2O and 0.2822 gram CO_2.

Found

	I.	II.	III.	IV.
C	-	-	-	45,51
H	-			3,77
S	-	2,03	2,13	
Cl.	29,10	-	-	

Action of acetic anhydride on octo resorcinol para-methyl sulphon phthaleïn:—

The phthaleïn was placed with a large excess of acetic anhydride in a flask fitted with a reflux condenser and

boiled vigorously for several hours, a green solution was formed, which afterwards turned black. On cooling, nothing separated, but when the liquid was cautiously poured into water, a black oil sank to the bottom, and soon turned to a solid mass. When filtered off and treated with caustic potash, a part dissolved with the characteristic fluorescence of the original phthaleïn, while the greater portion remained as a black, insoluble powder. Analysis gave carbon = 64.08 percent and hydrogen = 4.44 percent. No definite compound seems to have been formed.

Action of bromine on octo-resorcinal para methyl-sulphon-phthaleïn:- Two grams of the phthaleïn were treated in a small Erlenmeyer flask with a large excess of a a twenty percent solution of bromine in glacial acetic acid. Heat was at once produced. After about an hour's gentle warming on the water-bath, with the occasional addition of bromine solution had taken place, giving a dark red liquid from which on cooling amorphous crusts were deposited. The addition of water threw down a pink, finely-divided precipitate very hard to wash; the liquid was accordingly made alkaline and the substance in solution was precipitated by hydrochloric acid as a red substance resembling ferric hydroxide. A determination of

bromine gave 47.60 percent. A substituted ortho-resorcinol-para methyl-sulphon phthalein of the formula $C_{56}H_{35}Br_{11}O_{16}S$ would contain 46.8 percent of bromine.

A further endeavor to obtain a pure product was made. The same process was followed, the heating on the water-bath being succeeded by a heating in a sulphuric acid bath to the boiling point of the acetic acid. A compound similar to the first was formed, which gave the following analytical results:-

I. 0.1540 gram substance gave 0.0295 gram H_2O and 0.1943 gram CO_2.

II. 0.2171 gram substance gave 0.2507 gram AgBr.

	Calculated for	Found	
	$C_{56}H_{34}Br_{12}O_{16}S$	I	II
C	34.44	34.42	-
H	1.74	2.13	
Br	49.08		49.14

It seems that bromine easily enters the compound at first, but that this action takes place less readily as more and more enters, until prolonged action is necessary to force the last atoms into combination. These bromine substitution-products are very similar to eosin in their properties. They dissolve in alkalies with a dull red color, which when diluted shows the delicate fluorescence of the tetra-brom-fluorescein.

Action of Orcinol.

The action of orcinol upon ortho-sulpho-benzoic acid has been investigated by Mr. J. E. Gilpin, the results being published in his dissertation (1892). He obtained a di-orcinol- and a tetra-orcinol-phthaleïn of the acid, orcinol showing less readiness than resorcinol to enter into combination.

One equivalent of ortho-sulpho-para-toluic acid was heated with two equivalents of orcinol. The orcinol melted and dissolved the acid, but reaction was slow, being completed only after ten hours' heating at 170°. The resulting solid mass was powdered and washed with hot water, with which it does not become gummy. It was then treated in the usual manner.

I. 0.1774 gram substance gave 0.0734 gram H_2O

and 0.4197 gram CO_2.

II. 0.1747 gram substance gave 0.0744 gram H_2O and 0.4118 gram CO_2.

III. 0.2068 gram substance gave 0.1100 gram $BaSO_4$

	Calculated for (2 mol.) $C_{22}H_{18}O_6S$	Found I.	Found II.	Found III.
C.	64.39	64.52	64.28	
H.	4.39	4.60	4.73	
S.	7.80	—	—	7.31.

The substance seems to be a pretty pure di-orcinol-phthaleïn. It is a bright red powder, dissolving in alkalies with a red color and showing a green fluorescence considerably weaker than is the case with resorcinol phthaleïns. The field opened up by the formation of this compound is an interesting one, but its exploration was necessarily deferred.

Action of Hydroquinone.

Reaction between ortho-sulpho-para-toluic acid and hydroquinone does not readily take place, a compound being formed only after long continued heating. When the two substances in the molecular proportion of one to two were heated in the usual manner, a clear liquid was formed at 170°. At a temperature of 185° slight coloration began, accompanied by a gradual evolution of water. After about fifty hours, an opaque, viscous mass resulted, which on cooling formed a brittle black solid. It was purified in the usual way and analyzed with the following result:-

I. 0.1643 gram substance gave 0.0576 gram $BaSO_4$.

II. 0.1676 gram substance gave 0.0601 gram $BaSO_4$.

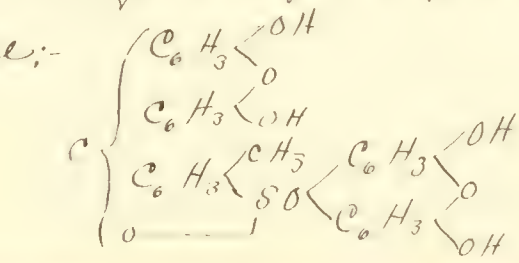
III. 0.1750 gram substance gave 0.0670 gram $BaSO_4$.

IV. 0.1617 gram substance gave 0.0582 gram H_2O and 0.3928 gram CO_2.

V. 0.1624 gram substance gave 0.0577 gram H_2O and 0.3935 gram CO_2.

	Calculated for (2 mol.) $C_{20}H_{14}O_6S$	Calculated for (4 mol.) $C_{32}H_{24}O_9S+H_2O$	I.	II.	III.	IV.	V.
C	63.09	65.75	–	–	–	66.25	66.17
H	3.66	4.12	–	–	–	4.00	3.95
S	8.38	5.47	4.90	4.93	5.26	–	–

It thus appears that a di-hydroquinone product is not formed, but instead, one containing four residues of the phenol. From the analogy of hydroquinone-phthaleïn the following may be given as a probable structure:-



Tetra-hydroquinone-para-methyl-sulphon phthaleïn is a compact, brown powder soluble in a large quantity of water with a yellow color. In alkalies it readily dissolves with a red color. Zinc dust and caustic potash reduce it to a nearly colorless solution.

Notwithstanding the difficulty of formation of the above compound, the use of other proportions may give yet other phthaleïns of hydroquinone.

Action of Pyrogallol.

An experiment is described by White in his dissertation, in which on heating together pyrogallol and orthosulpho benzoic acid he obtained a substance having properties like those of galleïn; the compound was not analyzed. Attempts described below to obtain a methyl sulpho-analogue of galleïn were successful, resulting in the formation of at least two phthaleïns.

Para methyl sulphon galleïn. - This compound was formed by heating together ortho-sulpho para-toluic acid and pyro-gallol in the molecular proportion of one to two. The clear liquid formed when these melted grew darker

and at 160° vigorous reaction took place. To prevent the mass from rising to the mouth of the tube, continuous stirring was necessary. After two hours' heating the product was a stiff substance that clung to the sides of the tube. On cooling it formed a brittle mass that when exposed to the air for any length of time became sticky. With water it formed a somewhat gelatinous mass that could not be filtered. It was then dissolved in caustic potash and re precipitated by hydrochloric acid, but it still packed on the filter paper. As an experiment the acidified mass was evaporated to dryness on the water-bath and the residue was powdered. It now presented more agreeable characteristics; it did not

become sticky in the air, and, this still rather easily soluble, the part not dissolved was easily filtered off and washed. The dried product gave the following analytical results:-

I. 0.1298 gram substance gave 0.0435 gram H_2O and 0.2649 gram CO_2.

II. 0.1274 gram substance gave 0.0426 gram H_2O and 0.2605 gram CO_2.

III. 0.1588 gram substance gave 0.0820 gram $BaSO_4$.

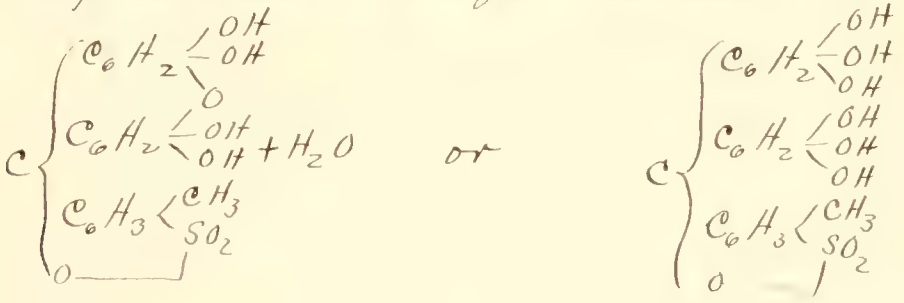
IV. 0.1477 gram substance gave 0.0749 gram $BaSO_4$.

V. 0.1361 gram substance gave 0.0701 gram $BaSO_4$.

	Calculated for	Found				
	$C_{20}H_{16}O_9S$	I.	II.	III.	IV.	V.
C	55.55	55.67	55.76	-	-	-
H	3.70	3.72	3.72	-	-	-
S	7.40	-	-	7.10	7.03	7.08

The fact that the percentages of carbon

are high, while sulphur comes persistently low, would indicate that a little of a higher derivative may have been mixed with the substance analyzed: this would cause the variation noted from the theoretical percentages. There seems to be no reason to doubt that an analogue of Baeyer's galleïn was obtained, which may be called para-methyl-sulphon galleïn, and which from analogy would have one of the following structural formulae:-



Owing to want of time no effort was made to decide between these possible structures by suitable experiments.

Para-methyl-sulphon-gallein is a black powder rather easily soluble in water, its dilute solution having a yellow color. If a drop of alkali be allowed to fall upon such a solution, a beautiful sky-blue color is produced. On stirring, and especially in more concentrated solutions, the blue is soon succeeded by a rich purple, often so deep as to appear black. An excess of acid brings back a yellow color, but the precipitate formed will not settle. When allowed to stand in the air, the alkaline solution gradually fades and becomes almost colorless, and a brown substance is deposited. The addition of a little stannous chloride prolongs the existence of the blue color.

Hexa-pyrogallol para methyl sulphon phthaleïn; One equivalent of the acid and four of the pyrogallol were heated in the usual manner, and reaction was even more vigorous than in the preceding case; After an hour's heating at 160° a solid mass resulted. On cooling it was brittle, and quickly became sticky. It presented in an aggravated form the difficulties encountered in the purification of para-methyl-sulphon-galleïn, but by the use of the same methods as were there employed, its purification was finally accomplished after a considerable loss on account of its solubility.

The most probable product from the reaction of the proportions used was a compound containing four

residues of pyrogallol. If, however, the reaction should take place as with resorcinol, a substance containing six such residues might be expected. Analysis showed that the latter was the case.

I. 0.1812 gram substance gave 0.0644 gram H_2O and 0.4001 gram CO_2.

II. 0.1740 gram substance gave 0.0615 gram H_2O and 0.3850 gram CO_2.

III. 0.2340 gram substance gave 0.0639 gram $BaSO_4$.

IV. 0.3566 gram substance gave 0.0995 gram $BaSO_4$.

	Calculated for ($C_{32}H_{22}O_{12}S$, 4 mol.)	Calculated for ($C_{44}H_{30}O_{16}S + 4\frac{1}{2}H_2O$, 6 mol.)	Found I.	II.	III.	IV.
C	60.90	60.47	60.22	60.34	-	-
H	3.49	3.78	3.94	3.92	-	-
S	5.08	3.66	-	-	3.75	3.83

When the proper proportions of ortho sulpho para-toluic acid and pyrogallol

are used, a product containing four residues may be expected; but no experiments were made with that object in view.

Hexa hydrogallol-para methyl sulphon phthaleïn is a black powder rather easily soluble in water and giving a rose color when such a solution is diluted. A drop of alkali gives a beautiful sky blue so evanescent as to be gone almost before it is seen. If some stannous chloride is added to a water solution of the phthaleïn and the alkali is then dropped in, the blue comes out beautifully and remains for some time. After the disappearance of the blue purple takes its place, and a perfectly colorless solution finally results.

Conclusions.

The results of the work done go to show that ortho-sulpho-para-tolnic acid forms three, poobably four, series of phthaleins with the phenols. Some of the members of the series are lacking, usually because an attempt to prepare them was not made, possibly in some cases because they cannot be formed. The series, so far as its members have been made, is as follows:

(a). Phenol-phthaleïns.

1. Di-phenol para-methyl sulphon phthaleïn.
2. Tetra-phenol para-methyl sulphon phthaleïn.

(b) Pyrocatechin phthaleïns.

4. octo-pyrocatechin para-methyl-sulphon-phthaleïn.

(c). Resorcinol-phthaleïns.

1. Para-methyl sulphon fluoresceïn.*

2. Tetra-resorcinol para methyl sulphon phthaleïn.*

3. Hexa-resorcinol-para-methyl-sulphon-phthaleïn.*

4. Octo-resorcinol para-methyl-sulphon-phthaleïn.

(d). Orcinol-phthaleïns.

1. Di-orcinol-para-methyl-sulphon-phthaleïn.

(e) Hydroquinone-phthaleïns.

2. Tetra-hydroquinone para methyl sulphon phthaleïn.

(f). Pyrogallol phthaleïns.

1. Para methyl sulphon galleïn.

2. Hexa-pyrogallol para methyl sulphon phthaleïn.

* First made by W. Jones.

Many interesting facts may be observed from this tabulation. It is seen that the phenols differ in their readiness to form phthaleïns, resorcinol being the only one with which a complete series has been thus prepared. Pyrocatechin, on the other hand, reacts most vigorously, going at once to the most complex derivatives. Pure substitution products have been difficult to prepare, bromine giving the best results. Treatment with phosphorus pentachloride results in the formation of a new class of compounds, whose nature is not apparent.

Biographical.

The author of this dissertation, James A. Lyman, was born October 17, 1866, in Lee county, Illinois. After receiving his early education in the public schools of the state, he entered Beloit College Academy, at Beloit, Wisconsin, in the fall of 1883. The following year he entered the freshman class of Beloit College, and received the degree of Batchelor of Arts in 1888. After a year of public school work, he studied chemistry at Beloit college for a year under the direction of Prof. E. G. Smith, to whom he would here express his thanks. Since October, 1890 he has pursued the study of Chemistry at the Johns Hopkins University. In 1891 he received the degree of Master of Arts from Beloit College.